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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/766,344	01/19/2001	Neil T. Parkin	59597-D/JPW/CMR	7661

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EXAMINER	
FOLEY, SHANON A	

ART UNIT	PAPER NUMBER
1648	13

DATE MAILED: 10/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/766,344	PARKIN ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *98-112,114-117 and 121* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *98-112, 114-117, 121* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

In paper no. 12, applicant amended claims 98, 101-107, 109-112, 114, 116, 117, and 121.

Priority

In response to the claim to priority, applicant states that the instant application already specifies a claim to priority. Applicant's priority claims have been reviewed, but do not contain any reference to the specific applications discussed in the previous Office action of paper no. 10 in the oath or the first line of the specification. Therefore, if applicant desires benefit to the co-pending applications, applicant must comply with 35 U.S.C. 119(a)-(e) and 120. If applicant does not desire benefit to priority and does not comply with 35 U.S.C. 119(a)-(e) and 120, applicant will only enjoy the benefit of priority to the application listed in the instant oath, i.e. 09/663,458.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 98-112, 114-117, and 121 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

Applicant states that the claims have been amended to indicate that the invention is a one step assay.

Applicant's amendment precipitates new grounds of rejection. The appended phrase to 98, 109, 114, and 117, drawn to the presence of a specific mutation indicating a change in susceptibility is unclear. A change would only be recognized if the sample is compared to a

previous sample by the same patient. In other words, if a sample is determined to have a codon mutation recited in the claims and is never compared with a sample from the same patient, how can it be determined whether the mutation resulted in a change of susceptibility or whether insensitivity to a protease inhibitor is inherent in the virus that the patient got infected with?

Applicant's amendment to claim 121 has been reviewed. However, the claim remains unclear in view of applicant's amendment. The claim states that the indicator gene indicates the presence or absence of the codon mutations. However, it is already known that the vector comprises a patient-derived segment comprising specific codon mutations, see lines 1-12 of the claim. Therefore, it is unclear why the indicator gene would be required in the vector since the presence of mutations is known.

Applicant's arguments regarding claim 100 have been considered, but are found unpersuasive. Claim 100 directly depends from claim 99, which does not recite "protease inhibitor". Therefore, it is maintained that claim 100 still lacks antecedent basis for "protease inhibitor" because the claim from which it directly depends does not recite these words.

Applicant did not address the rejections to claims 104 or 107-112 or amend the claims to obviate the rejections, all of which are still outstanding.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 98-102, 104, 105, 107, 108, 110, 112, and 114-116 are rejected under 35 U.S.C. 102(b) as being anticipated by Young et al. (The Journal of Infectious Diseases. Nov. 1998; 178(5): 1497-501) for reasons of record.

Applicant argues that the reference does not teach a method of detecting the instant mutations in an HIV nucleic acid.

Applicant's arguments and a careful review of the reference have been considered, but are found unpersuasive. In the "Methods" in the second column on page 1497, Young et al. teaches obtaining samples from HIV-infected patients and analyzing the nucleic acids obtained from the samples for drug resistance mutations. In Table 1 on page 1498, Young et al. teaches that an HIV-1 protease comprising a mutation at codon 82 (A, T, or F) and L90M, as well as specific secondary mutations leads to a change in susceptibility to indinavir, saquinavir, and/or amprenavir. Also in Table 1, Young et al. teaches that codon mutations in codons 90, 84, 82, 46, 10, and 54 correlate to an increase in sensitivity to indinavir and saquinavir. Therefore, Young et al. clearly anticipates every element in claims 98-102, 104, 105, 107, 108, 110, 112, and 114-116.

Claims 98-100 and 107-109 are rejected under 35 U.S.C. 102(b) as being anticipated by Hertogs et al. (Antimicrob. Agents Chemother. Feb. 1998; 42(2): 269-276) for reasons of record.

Applicant argues that the reference does not teach a method of detecting the instant mutations in an HIV nucleic acid.

Applicant's arguments and a careful review of the reference have been considered, but are found unpersuasive. In the "Materials and Methods" section on page 270, Hertogs et al. teaches method steps for determining phenotypic resistance to HIV protease inhibitors be

obtaining samples from HIV-infected patients, evaluating susceptibility to specific protease inhibitors in plasma-derived sequences, and determining the fold increase, which was greater than 10 fold in some instances, see Tables 5 and 6 on page 274. Hertogs et al. also teaches that mutations at codons 90 and 93 lead to correlate with drug resistance to indinavir and saquinavir, clearly anticipating claims 98-100 and 107-109.

Claim 117 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Young et al.

Applicant argues that the claim is not anticipated or rendered obvious in either Young et al. or Hertogs et al. because neither reference anticipates or suggests all of the specific mutations claimed.

Applicant's arguments as well as a review of the references have been considered, but are found unpersuasive. Applicant has amended the claim from its previous recitation, which precipitates new grounds of rejection based on this amendment. Claim 117 originally required that the nucleic acid be evaluated at codons 82 or 90 "and secondary mutations" listed (emphasis added). The amended claim now requires that the nucleic acid is evaluated for mutations at codons 82 or 90 and "**a** secondary mutation" to determine a change in susceptibility to a protease inhibitor (emphasis added). Therefore, since the claim has been amended to recite that codon 82 or 90 are evaluated in addition to one other codon, Young et al. anticipates the claim. See a summary of the teachings of Young et al. above. The reference teaches that a patient-derived HIV-1 protease comprising a mutation at codons 82 and 84 leads to a change in drug resistance to indinavir and saquinavir, see Table 1 on page 1498. Therefore, Young et al. clearly anticipates amended claim 117.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 121 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hertogs et al. as applied to claims 98-100 and 107-109 above, and further in view of Capon et al. (US 5,837,464) for reasons of record.

Applicant argues that Hertogs et al. does not teach or suggest the instant codon mutations and Capon et al. does not mention a codon mutation.

Applicant's arguments and a review of the references have been considered, but are found unpersuasive.

As demonstrated above, Hertogs et al. clearly anticipates the mutations recited in the claim. The reference does not suggest a test vector comprising an HIV patient-derived protease segment to determine changes in drug susceptibility, However, Capon et al. does, see the previous citations in the previous Office action as well as the description of Figure 8 D for example in column 17, lines 48-54. Therefore, the combined references teach every element in the claims.

There is also motivation to combine the references for reasons of record. One of ordinary skill in the art at the time the invention was made would have been motivated to express a patient-derived segment into a resistance test vector to amplify the genes that contain drug-resistant mutations so as not to deplete the primary source derived directly from the patient. One

of ordinary skill would be further motivated to express patient-derived segments into a test vector to simultaneously test different segments that may not be adjacent in the genome and spare the time and expense of generating recombinant viruses expressing mutations.

There is also a more than reasonable expectation for success in producing the instant invention because Capon et al. teaches introducing the test vector into host cells to determine drug resistance mutations, see claim 46, and Hertogs et al. teaches determining the presence of drug resistance by transforming recombinant viruses in tissue culture in the presence of drugs. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent evidence to the contrary.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley
October 18, 2002

JAMES HOUSEL 10/20/02
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600